

Sys-BodyFluid: a systematical database for human body fluid proteome research

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ABSTRACT

Recently, body fluids have widely become an important target for proteomic research and proteomic study has produced more and more body fluid related protein data. A database is needed to collect and analyze these proteome data. Thus, we developed this web-based body fluid proteome database Sys-BodyFluid. It contains eleven kinds of body fluid proteomes, including plasma/serum, urine, cerebrospinal fluid, saliva, bronchoalveolar lavage fluid, synovial fluid, nipple aspirate fluid, tear fluid, seminal fluid, human milk and amniotic fluid. Over 10 000 proteins are presented in the Sys-BodyFluid. Sys-BodyFluid provides the detailed protein annotations, including protein description, Gene Ontology, domain information, protein sequence and involved pathways. These proteome data can be retrieved by using protein name, protein accession number and sequence similarity. In addition, users can query between these different body fluids to get the different proteins identification information. Sys-BodyFluid database can facilitate the body fluid proteomics and disease proteomics research as a reference database. It is available at <http://www.biosino.org/bodyfluid/>.

INTRODUCTION

In the post-genome era, proteomic technology has rapidly developed to be a powerful platform for the research of human physiology. It can be applied for identifying potential novel biomarkers for prognosis, diagnosis and therapeutics (1,2). And in recent years it is shown that body

fluids have become one of the important targets for proteomics research (3). The body fluids include a wide variety of compositions like plasma/serum, urine, cerebrospinal fluid, saliva, bronchoalveolar lavage fluid, synovial fluid, nipple aspirate fluid, tear fluid, amniotic fluid and so on. Analysis of the protein composition in body fluids can help to understand human disease proteomics better. Hu *et al.*,(3) reviewed the body fluids research advances in proteome analysis and focused on its applications to human disease biomarker discovery. The importance of body fluids has also been appreciated by recent proteomics work (4). The database ‘MAPU: Max-Planck Unified database of organellar, cellular, tissue and body fluid’ (5) published in 2007 exhibit the close attention of the proteome researchers to the body fluids. The MAPU database stores the data from their own lab and contains several kinds of body fluids, such as urine and tear fluid. To collect more curated proteomics data in the related literatures of the body fluids and provide comprehensive protein annotation, as well as explore the relationships between the different body fluids, we constructed this database Sys-BodyFluid. Abundant proteomics data and in-depth protein annotation make Sys-BodyFluid to be a reference database for body fluid and clinical proteomics research.

DATABASE CONSTRUCTION

Sys-BodyFluid database was implemented through MySQL relational database (<http://www.mysql.com>). The web graphical user interface was constructed using JavaServer Pages technology (<http://java.sun.com/products/jsp/>). The manually curated body fluid protein data in the Sys-BodyFluid were imported to MySQL database by JAVA program. The protein annotation data were downloaded from International Protein Index (IPI) database, Gene Ontology (6), GOA database (7) and

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The authors wish it to be known that, in their opinion, the first three authors should be regarded as joint First Authors

Table 1. The data summary in Sys-BodyFluid database

Body fluid name	Protein number	Paper number
Plasma/Serum (11–23)	7748	13
Saliva (24–31)	2161	8
Urine (32–40)	1941	9
Cerebrospinal fluid (41–46)	1286	6
Seminal fluid (47,48)	916	2
Amniotic fluid (49–51)	899	3
Tear (52,53)	509	2
Bronchoalveolar lavage fluid (54,55)	411	2
Milk (56,57)	175	2
Synovial fluid (58)	114	1
Nipple aspiration fluid (59,60)	84	2
Total	10 138	50

KEGG (8) pathway database. Open source JAVA library named as JFreeChart (<http://www.jfree.org/jfreechart/>) distributed under LGPL was adopted to plot the image of the statistics data in the web.

DATA SOURCE AND DATABASE CONTENTS

We searched PubMed and manually curated 50 related peer-review publications published online before May 2008. The primary sequences of the proteins were retrieved by the original ID from their corresponding databases in these publications. Due to the database updates, the protein sequences reported in the literatures may have changed or depleted in the current databases. Therefore, these protein sequences were manually validated before importing into the database. Each protein was mapping to the IPI database to uniform the protein ID in Sys-BodyFluid by blasting these protein sequences against the database (Human IPI Version 3.44) (the *E*-value cutoff was set to 10^{-8} , the BLAST-HSP coverage was >0.9). Thus, each of the protein has a corresponding IPI ID in the Sys-BodyFluid database. The total unique proteins and paper numbers of the 11 kinds of body fluids in our database are summarized in Table 1. For example, there are 13 papers and 7748 proteins about the plasma/serum research in our database. Users can obtain this statistical information about the Sys-BodyFluid database in the ‘DATABASE’ web link in the website <http://www.biosino.org/bodyfluid>.

DATA AVAILABILITY

The Sys-BodyFluid is accessed from graphical web interface (<http://www.biosino.org/bodyfluid/>) and the data are available for download through the ‘DOWNLOAD’ link in the website as a text file. Users could specify their interested body fluid data to download.

DATABASE UTILITY

Sys-BodyFluid provides users the current database data statistics of different body fluids through the ‘DATABASE’ link for the paper number and the unique protein number (DATABASE Link). As shown in

Figure 1, Sys-BodyFluid offers users an optimal search function, including searching by protein ID, name and sequence similarity (SEARCH link, Figure 1A). The comprehensive browse option allows users to explore comparison analysis between two or more different body fluids data (Browse link, Figure 1B). For each protein in Sys-BodyFluid, we provide detailed annotation information, including protein description, involved body fluids, paper information, domain, Gene Ontology, pathway, sequence and so on (Figure 1C). Users can choose their interested body fluid to browse or download. Web page describing the body fluid provides users particular information. Furthermore, the availability of pathway analysis will assist users to investigate the difference between body fluids through involved metabolism and signal transduction pathway (Pathway link, Figure 1D). Proteins in our database are labeled with ‘red’ color. The body fluid number and paper number the proteins involved in are also showed in the web page.

RESULTS AND DISCUSSION

To get more comprehensive understanding of the relationship between body fluids, we compared the proteins composition in different body fluids. The result is shown in Figure 2A. There are 2928 proteins presented in at least two body fluids and 1359 proteins exist in at least three body fluids. Only 15 proteins exist in total 11 body fluids. For these 2928 proteins, GO annotation information were obtained and enrichment analysis was performed using BiNGO (9) and Cytoscape (10). Each node in Figure 2B represents a GO term. The node’s size is scaled by protein number and node’s color shows *P*-value of the enrichment analysis. The edge denotes the parent–children relationship between nodes. From this analysis, it is shown that some molecular functions like ‘protein binding’ and ‘enzyme regulator activity’ are over-presented in this dataset, as well as the biological process like ‘transport’ and ‘secretion’. Cellular component like ‘extracellular region’ is significantly enriched.

Human body fluids proteome analysis is still a challenge because dynamic range and the complexity of the body fluids protein composition. It is important to construct a body fluid reference database dedicated to biomarker discovery research. Previous work like MAPU is a great effort to integrate the data from their own lab and aim to provide a ‘gold standard’ reference proteome database. It is still necessary to refer to other proteomic literature data. For this reason, our database Sys-BodyFluid was build as a complementary database to the MAPU and aimed to provide users more information about the body fluids accompanied by protein abundant annotations. The relationship between different body fluids was also focused in our database. Users can access this database by <http://www.biosino.org/bodyfluid>.

PERSPECTIVES

As more and more body fluid proteome data have been produced recently, it is planned to update Sys-BodyFluid

A

Search In the Database:

Amniotic fluid
 Bronchoalveolar lavage fluid
 Cerebrospinal fluid
 Milk
 Nipple aspiration fluid
 Plasma/Serum

Search Protein by ID:

example

or Search Protein by Name:

example

or Search Protein by Sequence:

浏览...

B

Browse Proteins in given Body Fluid:

Plasma/Serum

Browse Proteins by Paper:

11425242: Detection and identification of human bronchoalveolar

Browse Proteins in two Body Fluids:

Plasma/Serum

Plasma/Serum

Browse Proteins in selected Body Fluids:

Plasma/Serum
 Urine
 Tear
 Cerebrospinal fluid
 Saliva
 Bronchoalveolar lavage fluid

C

IPI00163384

Summary

IPI	IPI00163384.6
Description	Retinol dehydrogenase 12
Body Fluid	Plasma/Serum : 1
Gene	145226
Master ID	SP:Q96NR8
Uniparc ID	UPI000001827
Other ID	ENSP00000267502;ENSG00000139988 HIT000011449;HX0011756 NP_689656;GI:18692839 Q96NR8;RDH12_HUMAN OTTHUHM00000028438;OTTHUHM00000029849

Annotation

Body Fluid	BodyFluid	SearchEngine
16047308	Plasma/Serum	SEQUEST

Domain

InterPro	Description	Start	End
IPR002198	Short-chain dehydrogenase/reductase SDR	40	177
IPR016040	NAD(P)-binding	37	240

Gene Ontology

GO ID	Description	Ontologies	Evidence
GO:0004745	retinol dehydrogenase activity	F	IDA
GO:0005488	binding	F	IEA
GO:0016491	oxidoreductase activity	F	IEA
GO:0042572	retinol metabolic process	P	IDA

KEGG Pathway

Pathway ID	Description
00051	Fructose and mannose metabolism
00052	Galactose metabolism
00120	Bile acid biosynthesis
00260	Glycine, serine and threonine metabolism

D

119 Proteins in KEGG pathway hsa04512

ProteinIPI	Description	GeneID	BodyFluid	Number	PaperNumber
IPI004117	Laminin subunit gamma-3 precursor	10319	1	2 (4.0%)	
IPI0001459	Chondroitin precursor	1101	2	3 (6.0%)	
IPI0029764	Collagen alpha-1(I) chain precursor	1277	5	10 (20.0%)	
IPI0030496	Collagen alpha-2(I) chain precursor	1278	5	11 (22.0%)	
	<i>&alpha;1-7</i> from <i>TGF-β</i>				

KEGG Pathway Map for hsa04512
(proteins in our database are labeled with red)

The diagram illustrates the ECM-RECEPTOR-INTERACTION pathway. It shows various proteins (red boxes) interacting with the Extracellular Matrix (ECM, grey boxes). These include integrins (VLA, Laminin), proteases (TACE, TEP1, Cathepsin, Plasminogen, Thrombin, Thrombospondin), and other proteins like CD44, CD45, and CD47. The pathways involve signaling cascades leading to cellular responses like proliferation and migration. A legend indicates that red proteins are from the database.

Figure 1. The web graphical user interface of Sys-BodyFluid database. (A) Search part and option. Users could search protein by protein ID, protein name and sequence similarity. (B) Browse part. Database allows user browse protein by their interested body fluid and interested paper. Protein existed in two body fluids could also be viewed and multi body fluids can be investigated. (C) Protein annotation part. There is detailed information in the database for each protein, including description, domain, Gene Ontology term, sequence and so on. (D) Pathway part. The proteins (colored by red) in different body fluids and their involved pathway are shown in pathway link. Proteins in our database are labeled with 'red' color. The body fluid number and paper number are also showed in the web page.

database every 6 months. New body fluid proteome data produced during the time will be added to our database. Furthermore, more annotation information like protein interaction data will also be included. In the future, we will collect more body fluid proteome

data in the disease proteomics research, for example, cancer and diabetes proteome data. If possible, tissue proteomics data will be also included to look into the crosstalk between the tissue protein and the body fluid protein.

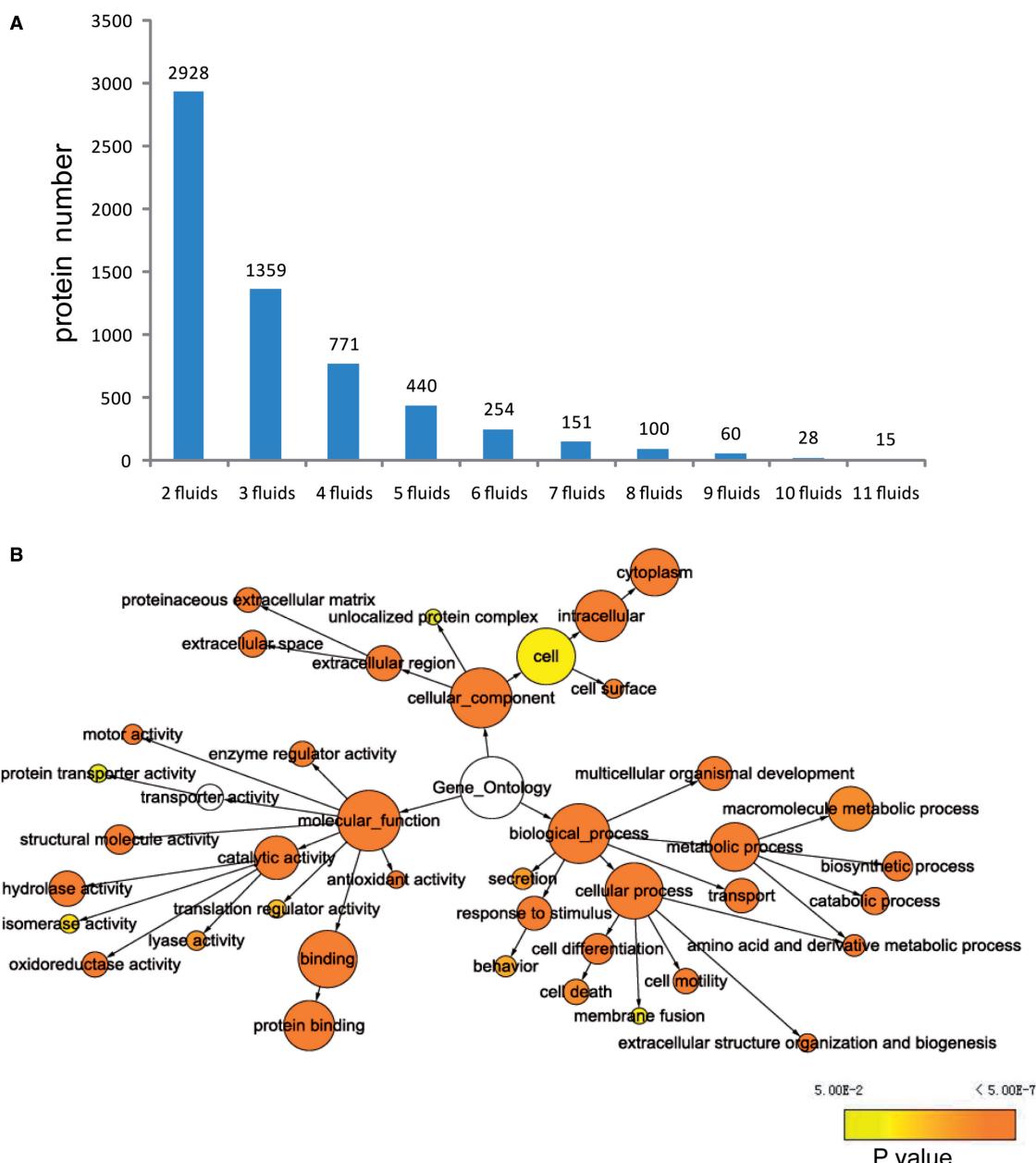


Figure 2. (A) The data comparison in different body fluids. There are 2928 proteins presented in at least two body fluids and 1359 proteins existed in at least three body fluids. Only 15 proteins exist in total 11 body fluids. (B) Gene Ontology annotation statistical analysis for the 2928 proteins existing in at least two body fluids.

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